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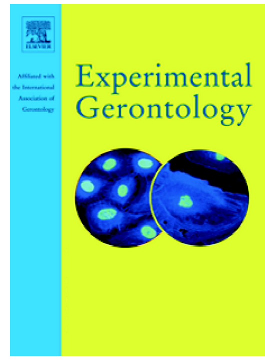

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Associations between markers of oxidative stress, skeletal muscle mass and function and to the influence of resistance exercise training, in older adults

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Abstract

Background: Oxidative stress (OS) negatively affects skeletal muscle homeostasis in experimental models of ageing. However, little is known about the associations between circulating OS markers and parameters of muscle mass and function, and their responses to exercise training, in humans.

Methods: Maximal voluntary contraction (MVC, primary outcome) and isokinetic torque of the knee extensors at 30° s^{-1} (MIT), muscle cross-sectional area (MCSA) and quality (MQ, secondary outcomes), and plasma concentrations of malondialdehyde (MDA, pro-OS), homocysteine (HCY, pro-OS), taurine (TAU, anti-OS), and protein sulfhydryl groups (PSH, anti-OS) were measured in 27 healthy older males and 23 females at baseline and after an 18-week resistance exercise program, with or without a nutritional intervention (fish oil vs. placebo).

Results: After adjusting for age, glomerular filtration rate, and nutritional intervention, there were no significant correlations between baseline OS markers and muscle parameters, barring a positive association between TAU and MIT in females (r=0.53, P=0.035) and between MDA and MCSA in males (r=0.69, P=0.001). Training did not significantly change OS markers, except for a reduction in MDA in females (-0.27 μmol/L, 95% CI -0.51 to -0.02, P=0.034). In females, there were significant correlations between baseline MDA and exercise-induced changes in MVC (P=0.018), baseline TAU and changes in MCSA (P=0.026), and baseline HCY and changes in MCSA (P=0.046) and MQ (P=0.022). In males, baseline MDA was significantly associated with exercise-induced changes in MVC (P=0.040).

Conclusions: Plasma MDA, HCY, and TAU were significantly associated with baseline and/or exercise-induced changes in muscle mass and function in healthy older adults, primarily in females. Pending further confirmation in other populations, specific OS markers, particularly MDA, might predict muscle responses to resistance exercise programs in old age.

Key words: oxidative stress, muscle mass, muscle function, old age, exercise.

1. Introduction

Ageing is associated with intracellular and extracellular morphological and functional changes, resulting in the progressive impairment of organ function and the development of disease states. One typical example is the significant decline in neuromuscular function and performance associated with the reduction of skeletal muscle mass (sarcopenia), which results in impaired muscle strength and physical performance (Hunter et al., 2016, Cruz-Jentoft et al., 2010, Morley et al., 2011). The estimated prevalence of sarcopenia in old age ranges between 25-50% (Patel et al., 2013). The progressive increase in the number of frail older adults will inevitably lead to an increased prevalence of sarcopenia, and its associated health-care costs, worldwide (Muscaritoli et al., 2010, Visser and Schaap, 2011).

Many factors have been proposed to play a role in the pathogenesis of sarcopenia, including physical inactivity, alterations in protein metabolism and hormones, neurodegeneration, inflammation, and oxidative stress (OS) (Rolland et al., 2008). There is good evidence that the process of ageing is associated with increased concentrations of reactive oxygen and/or nitrogen species (RONS), and a reduction in endogenous antioxidants, in the skeletal muscle (Reid and Durham, 2002). This can lead to modifications of nucleic acids, proteins and lipids, resulting in molecular damage and/or dysfunction.

High concentrations of RONS have been shown to negatively affect muscle mass and function by altering the balance between protein synthesis and proteolysis (Fulle et al., 2004, Powers et al., 2011). However, the assessment of the effect of OS on skeletal muscle homeostasis has primarily been conducted in *in-vitro* studies and animal models, and the generalizability of these findings in humans is uncertain (Ji, 2015, Scicchitano et al., 2017). The investigation of circulating markers of OS in older adults might be particularly useful for the identification of those at risk of developing sarcopenia and/or responders to specific interventions, such as exercise training.

The aim of this study was to investigate the associations between predefined pro-OS and anti-OS markers and established parameters of skeletal muscle mass and function, and their responses to an exercise training and nutritional intervention program, in healthy older adults. Since the direct measurement of OS markers in tissue or body fluids is challenging, we measured plasma concentrations of oxidation target products such as malondialdehyde (MDA), low molecular thiol (HCY), and the antioxidants sulfhydryl group of proteins (PSH) and taurine (TAU). We hypothesized that plasma concentrations of pro-OS and anti-OS markers were associated, respectively, with lower and higher skeletal muscle mass and function at baseline, and their adaptations to exercise.

2. Methods

2.1. Study population

We recruited 50 community-dwelling adults >65 years old (27 males and 23 females) that were not participating in any resistance exercise training, had no history of cardiovascular disease, cancer, arthritis, respiratory disease, metabolic disease, recent fractures and loss of mobility, and did not take regular analgesics or nutritional supplements. However, one female was prescribed angiotensin converting enzyme inhibitors for mild hypertension, and one male was prescribed allopurinol for gout. The study was approved by the University of Aberdeen College of Life Sciences and Medicine Ethics Review Board (CERB/2011/6/644) and registered at clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT02843009). Written consent was obtained after explaining the aims, risks, and potential discomfort, in accordance with the declaration of Helsinki. Participants were part of a study investigating the effects of fish oil consumption on adaptations to 18 weeks of resistance exercise training, and were randomly assigned to either 3.0 g/day safflower oil or 3.0 g/day fish oil with data on other aspects of the project published elsewhere (Da Boit et al., 2017). All the measurements were taken at baseline and at the end of the 18 week intervention.

2.2. Resistance exercise training

Resistance exercise training was performed twice weekly for 18 weeks. Each session included four sets of nine repetitions for each exercise: leg press, leg extension, leg curl and calf press. The load for each exercise was set at 70% of the participant's one repetition maximum (1RM). This was assessed for each exercise at baseline and every six weeks, and the load adjusted accordingly.

2.3. Parameters of muscle mass and function

The following measurements were performed the morning after an overnight fast, as previously described (Da Boit et al., 2017). Measurements were made prior to and at least 48-h after the completion of the resistance exercise training intervention.

2.3.1. Knee extensor isometric and isokinetic torque

The maximal isometric torque of the knee extensor muscles of the right leg was determined during a maximal voluntary contraction (MVC) with the participant seated on a Biodex dynamometer with a knee angle of 73°. With the same seating position, maximal isokinetic torque (MIT) of the knee extensors was measured at 30° s^{-1}.

2.3.2. Magnetic resonance imaging (MRI)

Forty-five participants underwent MRI (3 others were claustrophobic and 2 had metal implants) on a Philips Achieva 3.0 Tesla whole body scanner using a 16-channel SENSE XL Torso coil. Muscle cross-section area (MCSA) was quantified mid-thigh. Muscle quality (MQ) was calculated as torque (knee extensor isometric strength) per unit MCSA.

2.4. Anthropometric and OS parameters

Body weight and height were measured, and body mass index (BMI) calculated, for each study participant at baseline. Blood samples were collected by venipuncture in K^+ EDTA vacutainers, placed on ice and processed within 30 min. After samples were centrifuged for 10 min at 4 °C at 800*g* plasma was aliquoted and stored at -80°C until analysis. MDA was determined by spectrophotometry according to an established method (Esterbauer and Cheeseman, 1990). Briefly, plasma was mixed with 0.075% thiobarbituric acid and incubated at 95 °C for 30 min. MDA concentration was assayed by measuring the absorbance at 535 nm using a MDA standard curve. Protein–SH (PSH) was assessed by spectrophotometry at 405 nm using 5,5', dithiobis-2-nitrobenzoic acid (Ellman, 1959). PSH concentration was determined using a glutathione standard curve and then normalized versus protein plasma quantity measured by the Lowry's method. The low molecular weight thiols HCY, and TAU were determined by capillary electrophoresis (CE) with Laser Induced Fluorescence detection (Carru et al., 2004, Zinellu et al., 2003, Zinellu et al., 2009). Following protein precipitation with trichloroacetic acid, samples were derivatized using 5-(Iodoacetamido)fluorescein as fluorophore for HCY, and with fluorescein isothiocyanate for TAU. Following dilution, samples were injected in CE. Plasma creatinine and creatine concentrations were measured using an Aquity UPLC coupled to a qToF Premier high-resolution mass spectrometer (Waters, Sydney, Australia). Estimated glomerular filtration rate (eGFR) was measured using the Modification of Diet in Renal Disease formula (Levey et al., 1999).

2.5. Statistical analysis

Results are expressed as means ± SD, medians and interquartile ranges, or frequencies as appropriate. After testing for normal distribution, using the Kolmogorov-Smirnov test, between-group differences were assessed either by one-way ANOVA or Mann-Whitney U test. Differences between baseline and post-exercise muscle mass and function were assessed either by paired Student's *t*-test or Wilcoxon test. In each sex, the effects of exercise and nutritional intervention on OS markers were assessed by ANCOVA. Partial correlations, adjusted for age, eGFR, and nutritional intervention, assessed the relationship between baseline OS markers and parameters of skeletal muscle mass and function, and their changes after the exercise training (MVC: primary outcome; MIT, MCSA and MQ: secondary outcomes). Analyses were performed using IBM SPSS Statistics Version 23, Release 23.0.0.2 (SPSS Inc., Armonk, NY, USA). A two-sided $P<0.05$ indicated statistical significance.

3. Results

3.1. Baseline characteristics

MVC, MIT, MCSA, and plasma creatinine, HCY and PSH concentrations were significantly higher in males. By contrast, plasma creatine concentrations were significantly higher in females (Table 1). MQ and TAU and MDA concentrations were similar in both sexes.

3.2. Effect of exercise on muscle parameters and OS markers

The resistance exercise training program significantly increased MVC (31±24%, $P<0.001$), MIT (12±18%, $P<0.001$), MCSA (3±5%, $P<0.001$) and MQ (27±26%, $P<0.001$) in the whole group. There were no significant exercise-induced changes in OS markers, except for a significant reduction in MDA concentrations in females (Table 2).

3.3. Females

3.3.1. Baseline

There were no significant correlations between OS markers and parameters of muscle mass and function, barring a significant positive correlation between TAU and MIT (Table 3).

3.3.2. Exercise-induced changes

There was a significant positive correlation between baseline HCY and changes in MCSA, and a negative correlation between baseline HCY and changes in MQ (Table 4). Significant positive correlations were also observed between baseline TAU and changes in MCSA, and between baseline MDA and changes in MVC (Table 4).

3.4. Males

3.4.1. Baseline

There were no significant correlations between baseline OS markers and muscle parameters, barring a significant positive association between MDA and MCSA (Table 5). Such an association was not observed in females, in whom a significant positive correlation between TAU and MIT was found; the latter association was not seen in males.

3.4.2. Exercise-induced changes

There were no significant correlations between baseline OS markers and changes in muscle parameters, barring a significant positive association between MDA and changes in MVC (Table 6). Such a positive correlation was observed also in females, as mentioned above.

4. Discussion

Many efforts have been recently made to identify effective strategies to prevent and treat sarcopenia, including targeted pharmacological treatments, hormone replacement therapies, antioxidant-nutritional interventions, and physical exercise (Cruz-Jentoft et al., 2010, Morley et al., 2011). Among them, physical exercise has been shown to be particularly effective by increasing muscle strength, mass, and physical performance (Yoshimura et al., 2017). The identification of circulating biomarkers associated with parameters of muscle mass and function would be useful not only for sarcopenia risk stratification but also to predict the response to exercise training programs in older adults.

In this study, we investigated associations between predefined markers with either pro-OS or anti-OS activity and parameters of muscle structure and function, at baseline and after a resistance exercise training and nutritional intervention program, in a group of healthy older adults. At baseline, there were no significant correlations between OS markers and muscle parameters, except for a positive association between TAU and MIT in females and between MDA and MCSA in males. There were no significant exercise-induced changes in the concentrations of OS markers in either sex, except for a significant reduction in MDA in females. In females, there were significant correlations between baseline MDA and exercise-induced changes in MVC, TAU and changes in MCSA, and between baseline HCY and changes in MCSA and MQ. In males, baseline MDA was significantly associated with exercise-induced changes in MVC. Therefore, the pro-OS MDA and HCY and the anti-OS TAU, but not PSH, showed significant associations with baseline and/or exercise-induced changes in skeletal muscle mass and function. In particular, baseline MDA concentrations predicted exercise-induced changes in MVC, the primary outcome, in both sexes.

MDA, the enzymatic and non-enzymatic product of prostaglandins breakdown, endoperoxide, and the end product of lipid peroxidation (Ayala et al., 2014), is useful for the monitoring of serum free radicals. The latter are difficult to measure directly because of their relatively low stability. Animal and human studies have investigated the effects of chronic (weeks to months) exercise on MDA concentrations. However, in these studies it was not possible to investigate the associations between plasma/serum MDA and skeletal muscle parameters because a) MDA concentrations were measured in specific tissues, and b) parameters of muscle mass and function were not assessed. Ravi Kiran et al. studied the effects of different intensities and durations of swim training sessions, six days/week for four weeks, on myocardial MDA concentrations in young and old rats. A significant exercise-induced reduction in myocardial MDA concentrations was observed in both groups (Ravi Kiran et al., 2006). Pangkahila et al. studied the effects of eight-week conventional training or balanced physical exercise on serum MDA, but not muscle parameters, in 24 males aged 18-30 years. MDA concentrations, measured before and after a training session at baseline and eight weeks later, were not significantly different over time and between the groups (Pangkahila et al., 2016). In our study, the exercise-associated reduction in plasma MDA concentrations was statistically significant in females but not in males. This suggests that resistance exercise training might have beneficial effects on lipid peroxidation in older individuals, particularly women. However, the observed reduction in MDA concentrations might also be an indirect result of the improvement in the control of free radical production by the mitochondria (Daussin et al., 2012). Notably, the observed associations between baseline MDA concentrations and changes in MVC, after the resistance exercise intervention, in both sexes support the potential predictive role of MDA. Baseline elevations in MDA concentrations could identify subjects exhibiting a greater MVC response after resistance exercise training. This identification of those individuals that are more likely to respond, could predict the outcome of exercise programs in specific patient groups. Moreover, the identification of non-responders might lead to the identification of either impaired muscle homeostasis and/or risk of sarcopenia in old age. By contrast, the exercise program exerted opposite, albeit not significant, effects on plasma TAU concentrations in males (decreased) and females (increased). Baseline TAU concentrations were significantly correlated with baseline MIT and with exercise-induced changes in MCSA in females, but not in males. TAU plays an important role in several physiological functions, including cell signaling and development, membrane stability and receptor regulation, and various antioxidant and metabolic effects (Huxtable, 1992). Furthermore, it regulates the release of Ca^{2+} from the sarcoplasmic reticulum and maintains the sensitivity of contractile elements to Ca^{2+}, affecting directly the excitation-contraction process and skeletal muscle strength (Spriet and Whitfield, 2015).

Animal and human studies have previously investigated the effects of TAU supplementation on skeletal muscle mass and function and the effects of acute exercise on TAU concentrations, however no study has sought to determine the effects of chronic exercise on TAU concentrations in humans. In our study, 18-weeks of resistance exercise training significantly increased all parameters of skeletal mass and function in males, despite the trend towards a reduction in plasma TAU concentrations. This suggests that TAU concentrations are unlikely to play a significant role in the observed exercise-induced changes in muscle parameters in this group. By contrast, the significant correlations between baseline TAU and exercise-induced changes in MCSA in females suggest, similarly to MDA, a potential role of this sulfur-containing β-amino acid in the identification of female responders to exercise training programs.

Resistance exercise training did not significantly change plasma HCY concentrations in both sexes. However, baseline plasma HCY concentrations were positively associated with exercise-induced changes in MCSA, and negatively associated with changes in MQ, in females but not in males. Human studies have previously investigated the associations between HCY concentrations, physical exercise, and muscle strength. Steenge et al reported a non-significant reduction in plasma HCY concentrations (-0.6 μmol/L, 95% CI -1.9 to 0.5) in healthy women aged 19-38 years undergoing an eight-week period of resistance exercise, with three sessions each week involving leg squats, leg presses, leg curls, leg rowing, leg extensions, shoulder presses, sit-ups, and step-up exercises (Steenge et al., 2001). In a cross-sectional study, Kuo et al observed a significant negative association between plasma HCY concentrations and peak quadriceps strength in 1,677 older adults from the National Health and Nutrition Examination Survey 1999-2002 (Kuo et al., 2007). In another cross-sectional study of 2,919 older adults with hyperhomocysteinemia, Swart et al reported that plasma HCY concentrations were not independently associated with skeletal muscle mass, however they were independently associated with reduced handgrip strength in women (P=0.02) but not in men (Swart et al., 2013a). By contrast, in a study of 1,301 older adults from the Longitudinal Aging Study in Amsterdam, Swart et al observed an independent negative association between plasma HCY concentrations and reduced handgrip strength in men (P<0.01) but not in women. However, HCY concentrations did not predict the changes in handgrip strength after a three-year follow up (Swart et al., 2013b). We did not observe any significant correlation between plasma HCY concentrations and baseline and exercise-induced changes in parameters of muscle strength, MVC and MIT, in both sexes. However, similarly to TAU, the correlations with changes in MCSA and MQ in females warrant further research to clarify the potential predictive role of this highly reactive and pro-oxidant amino acid in subjects undergoing exercise training programs.

Although baseline PSH concentrations were significantly higher in males than in females, we did not observe any significant exercise-induced changes in PSH concentrations, or associations between PSH and parameters of muscle mass and function. In accordance to our findings, Margaritis et al did not observe any significant change in PSH concentrations in five healthy young males undergoing a six-month training program consisting of 29 training sessions, performed every three days, involving two types of exercise, the squat and the calf press. No specific parameters of muscle mass and function were assessed (Margaritis et al., 2009). Pending further confirmation in longitudinal studies, our results do not suggest a significant role of PSH in terms of sarcopenia risk stratification and identification of responders to exercise training programs, based on changes in muscle strength, volume, and quality.

The observation of sex-related differences in the markers studied, particularly TAU and HCY, suggests that the relationship between antioxidant and lipid peroxidation pathways and skeletal muscle homeostasis may be sex-specific.

Indeed, other studies reported variances in different markers of oxidative stress between sexes. These differences were not related to dissimilarities in hormones between sexes (Tóthová et al., 2013; Kander et al., 2017). This can have a different impact on muscle function and adaptation to exercise, and might also help in the identification of tailored exercise programs in older males and females.

Moreover, the capacity of MDA to predict exercise-induced changes in MVC in both sexes suggests that this OS marker can predict treatment responders and that therapies targeting MDA and specific OS pathways might provide salutary effects on skeletal muscle homeostasis in old age. Furthermore, altered MDA concentrations could predict the noxious effects of exaggerated physical activity in over-trained older individuals, especially if non-athletes, in accordance with existing evidence in younger cohorts (Margonis et al., 2007; Palazzetti et al., 2003).

Our study has some limitations, including its relatively small sample size and the recruitment of participants without significant medical history. Therefore, it is unknown whether our results can be generalized to other older populations, particularly frail patients with sarcopenia. Nevertheless, it also has significant strengths, including the rigorous assessment of established pro- and anti-OS markers and established parameters of muscle mass and function. Furthermore, we ruled out the potential confounding effect of co-morbidities and medications that can affect skeletal muscle structure and function, and closely supervised the exercise training program in all participants.

In conclusion, the pro-oxidant markers MDA and HCY and the anti-oxidant marker TAU showed significant associations with baseline and/or exercise-induced changes in skeletal muscle mass and function in healthy older adults, particularly in females. Pending further confirmation in other study populations, these markers might be useful for sarcopenia risk stratification and prediction of responses to resistance exercise programs.

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Table 1. Baseline characteristics

Parameter	**Whole group (n=50)**	**Males (n=27)**	**Females (n=23)**	**P-value***
Age (years)	70 [67, 73]	69 [67, 72]	71 [68, 73]	0.544
Height (cm)	169 [159, 176]	175 [172, 179]	159 [155, 168]	**<0.0001**
Weight (Kg)	72.1±15.1	78.1±15.0	65.1±12.3	**0.002**
BMI (Kg/m^2)	25.4±4.4	25.6±4.2	25.3±4.7	0.821
eGFR (mL/min)	80±12	77±12	83±13	0.079
Creatine (μmol/L)	168±76	134±51	208±83	**0.001**
Creatinine (μmol/L)	79±12	85±10	71±9	**<0.0001**
MVC (N•m)	90 [75, 120]	115 [94, 138]	76 [68, 85]	**<0.0001**
MIT (N•m)	116±37	141±32	86±14	**<0.0001**
MCSA (cm^2)	51 [38, 64]	63 [58, 68]	37 [32, 43]	**<0.0001**
MQ (N•m/cm^2)	2.0±0.5	1.9±0.5	2.1±0.5	0.293
HCY (μmol/L)	13.6±3.7	14.8±4.2	12.4±2.6	**0.031**
TAU (μmol/L)	57.7±20.3	61.8±25.2	53.1±11.8	0.156
MDA (μmol/L)	2.78±0.59	2.93±0.53	2.61±0.63	0.067
PSH (μmol/L)	5.47±0.82	5.88±0.77	5.03±0.64	**0.0001**

Data shown as mean ± SD or median [IQR] as appropriate

BMI, body mass index; eGFR, estimated flomerular filtration rate; MVC, maximal voluntary contraction; MIT, maximal isokinetic torque; MCSA, muscle volume; MQ, muscle quality; HCY, homocysteine; TAU, taurine; MDA, malondialdehyde; PSH, sulphydril group of protein.

Significant differences (P<0.05) are highlighted in bold.

Table 2. Baseline vs. post-exercise mean (95% CI) differences in oxidative stress markers in females and males

	Mean (95% CI) difference	**P-value**
Females		
HCY	+0.15 (-0.57 to 0.86)	0.673#
TAU	+4.24 (-1.67 to 10.16)	0.149
MDA	-0.27 (-0.51 to -0.02)	**0.034**
PSH	-0.19 (-0.41 to 0.03)	0.094
Males		
HCY	+0.25 (-0.75 to 1.25)	0.613
TAU	-7.06 (-16.08 to 1.95)	0.119
MDA	-0.09 (-0.28 to 0.11)	0.356
PSH	+0.07 (-0.21 to 0.36)	0.600

HCY, homocysteine; TAU, taurine; MDA, malondialdehyde; PSH, sulphydril group of protein.

Significant differences (P<0.05) are highlighted in bold.

#, time * nutritional intervention interaction (P<0.05)

Table 3. Partial correlations* between baseline oxidative stress markers and parameters of muscle mass and function in females

	MVC (N•m)	**MIT (N•m)**	**MCSA (cm^2)**	**MQ (N•m.cm^2)**
HCY	r= +0.143 P=0.597	r= +0.004 P=0.988	r= -0.447 P=0.082	r= +0.476 P=0.062
TAU	r= +0.140 P=0.58	**r= +0.53** **P=0.035**	r= +0.093 P=0.732	r= +0.073 P=0.789
MDA	r= -0.448 P=0.081	r= +0.003 P=0.99	r= +0.021 P=0.939	r= -0.348 P=0.186
PSH	r= +0.101 P=0.711	r= +0.384 P=0.142	r= +0.1 P=0.713	r= +0.055 P=0.841

*, adjusted for age and estimated glomerular filtration rate

MVC, maximal voluntary contraction; MIT, maximal isokinetic torque; MCSA, muscle volume; MQ, muscle quality; HCY, homocysteine; TAU, taurine; MDA, malondialdehyde; PSH, sulphydril group of protein.

Significant correlations (P<0.05) are highlighted in bold.

Table 4. Partial correlations* between oxidative stress markers and percent exercise-induced changes in parameters of muscle mass and function in females

	Δ%MVC (N•m)	**Δ%MIT (N•m)**	**Δ%MCSA (cm^2)**	**Δ%MQ (N•m.cm^2)**
HCY	r= -0.155 P=0.582	r= +0.066 P=0.816	**r= +0.522** **P=0.046**	**r= -0.585** **P=0.022**
TAU	r= +0.278 P=0.316	r= -0.112 P=0.692	**r= +0.573** **P=0.026**	r= -0.009 P=0.974
MDA	**r= +0.6** **P=0.018**	r= -0.105 P=0.709	r= +0.036 P=0.898	r= +0.093 P=0.741
PSH	r= +0.198 P=0.480	r= -0.258 P=0.353	r= +0.355 P=0.194	r= -0.404 P=0.135

*, adjusted for age, estimated glomerular filtration rate, and nutritional intervention
MVC, maximal voluntary contraction; MIT, maximal isokinetic torque; MCSA, muscle volume; MQ, muscle quality; HCY, homocysteine; TAU, taurine; MDA, malondialdehyde; PSH, sulphydril group of protein.
Significant correlations (P<0.05) are highlighted in bold.

Table 5. Partial correlations* between baseline oxidative stress markers and parameters of muscle mass and function in males

	MVC (N•m)	MIT (N•m)	MCSA (cm^2)	MQ (N•m.cm^2)
HCY	r= +0.208 P=0.38	r= +0.151 P=0.526	r= +0.303 P=0.194	r= +0.72 P=0.762
TAU	r= -0.111 P=0.641	r= +0.316 P=0.175	r= -0.407 P=0.075	r= +0.321 P=0.167
MDA	r= +0.221 P=0.349	r= +0.293 P=0.211	**r= +0.699 P=0.001**	r= -0,122 P=0.608
PSH	r= -0.179 P=0.451	r= -0.130 P=0.585	r= +0.341 P=0.141	r= -0.367 P=0.111

*, adjusted for age and estimated glomerular filtration rate

MVC, maximal voluntary contraction; MIT, maximal isokinetic torque; MCSA, muscle volume; MQ, muscle quality; HCY, homocysteine; TAU, taurine; MDA, malondialdehyde; PSH, sulphydril group of protein.

Significant correlations (P<0.05) are highlighted in bold.

Table 6. Partial correlations* between oxidative stress markers and percent exercise-induced changes in parameters of muscle mass and function in males

	Δ%MVC (N•m)	**Δ%MIT (N•m)**	**Δ%MCSA (cm^2)**	**Δ%MQ (N•m.cm^2)**
HCY	r= +0.387 P=0.101	r= +0.303 P=0.208	r= +0.113 P=0.645	r= +0.341 P=0.153
TAU	r= -0.043 P=0.86	r= -0.026 P=0.916	r= +0.388 P=0.101	r= -0.13 P=0.595
MDA	**r= +0.475 P=0.04**	r= +0.226 P=0.353	r= +0.019 P=0.937	r= +0.44 P=0.06
PSH	r= -0.93 P=0.705	r= -0.187 P=0.444	r= -0.184 P=0.451	r= -0.46 P=0.852

*, adjusted for age, estimated glomerular filtration rate, and nutritional intervention

MVC, maximal voluntary contraction; MIT, maximal isokinetic torque; MCSA, muscle volume; MQ, muscle quality; HCY, homocysteine; TAU, taurine; MDA, malondialdehyde; PSH, sulphydril group of protein.

Significant correlations (P<0.05) are highlighted in bold.

Dear Editor,

you will find here the **Highlights** of the original manuscript entitled "**Associations between markers of oxidative stress, skeletal muscle mass and function and to the influence of resistance exercise training, in older adults**" by Mariasole Da Boit, Panagiotis Paliogiannis, Angelo Zinellu, Salvatore Sotgia, Rachael Sibson, Judith R. Meakin, Richard M. Aspden, Arduino A. Mangoni, Stuart R. Gray and my self.

Highlights

- TAU and HCY, suggests that the relationship between antioxidant and lipid peroxidation pathways and skeletal muscle homeostasis may be sex-specific.
- Resistance exercise training did not significantly change plasma HCY concentrations in both sexes
- Plasma MDA, HCY, and TAU were significantly associated with baseline and/or exercise-induced changes in muscle mass and function in healthy older adults, primarily in females